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FACSIMILE TRANSMISSION

September 22, 2005

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TO	FROM
USPTO	Cynthia J. Lee
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RE: *Re: U.S. Utility Patent Application*
Serial No.: 09/632,639; Filing Date: July 31, 2000
Title: Inhibition of Target-Mediated Cross-Hybridization
Inventor(s): Jeffery R. Sampson, et al.

(Message)

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AGILENT TECHNOLOGIES, INC.
Legal Department, DL429
Intellectual Property Administration
P. O. Box 7599
Loveland, Colorado 80537-0599

ATTORNEY DOCKET NO. 10992786-1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventor(s): Jeffrey R. Sampson et al.

Serial No.: 09/632,639 **Examiner: Zara, Jane J.**

Filing Date: July 31, 2000 **Group Art Unit: 1635**

Title: Inhibition of Target-Mediated Cross-Hybridization

COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria VA 22313-1450

TRANSMITTAL OF REPLY BRIEF

Sir:

Transmitted herewith is the Reply Brief with respect to the Examiner's Answer mailed on This Reply Brief is being filed pursuant to 37 CFR 1.193(b) within two months of the date of the Examiner's Answer.

(Note: Extensions of time are not allowed under 37 CFR 1.136(a))

(Note: Failure to file a Reply Brief will result in dismissal of the Appeal as to the claims made subject to an expressly stated new grounds of rejection.)

No fee is required for filing of this Reply Brief.

If any fees are required please charge Deposit Account **50-1078**.

Respectfully submitted,

Jeffrey R. Sampson et al.

By Cynthia J. Lee

Cynthia J. Lee
Attorney/Agent for Applicant(s)

Reg. No. 45,033

Date: September 22, 2005

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BOARD OF PATENT APPEALS AND INTERFERENCES

In Re Application of:

Jeffrey R. Sampson *et al.*

Confirmation No.: **3760**

Group Art Unit: **1635**

Serial No.: **09/632,639**

Examiner: **Zara, Jane J.**

Filed: **July 31, 2000**

Docket No.: **10992786-1**

For: **Inhibition of Target-Mediated Cross-Hybridization**

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September 22, 2005 — Jennifer Pomonis
Date

REPLY TO EXAMINER'S ANSWER

Mail Stop Appeals - Patents
Commissioner of Patents and Trademarks
P.O. Box 1450
Alexandria, Virginia 22313-1450

Sir:

The Examiner's Answer mailed July 25, 2005 has been carefully considered. In response thereto, please consider the following remarks.

REMARKS

The Examiner has provided in the Examiner's Answer various responses to arguments contained in Applicants' Appeal Brief. Applicants address those responses in the following. Applicants note for the record that to the extent that every argument presented in Applicants' Appeal Brief that was not addressed in the Examiner's Answer, Applicants incorporate each of those arguments by reference into the present Reply Brief.

I. Withdrawal of Rejection based on *Vivekanada et al.*

Applicants appreciate Examiner's careful consideration of Applicants' arguments submitted in the Appeal Brief, and the withdrawal of the rejection of claims 1-26 under 35 U.S.C. §102(e) over U.S. Patent No. 6,569,630 issued to *Vivekananda et al.*

II. Reply to Examiner's Argument Regarding *Kutyavin et al.*

Applicants continue to fundamentally disagree with the Examiner's position that the cited reference, U.S. Patent No. 5,912,340 issued to *Kutyavin et al.*, discloses the methods and kit for synthesizing nucleic acid molecules as claimed. In addition to the remarks set forth in Applicants' Appeal Brief, Applicants offer the following additional comments, which they hope will be useful to the Board.

1. First, Applicants object to the Examiner presenting many arguments for the first time in Answer to Applicants' Appeal Brief. Applicants submit that these arguments should have been raised during prosecution of the application prior to appeal. For example, the Examiner's arguments with respect to the abstract of *Kutyavin et al.* on page 5 of the Answer, and the arguments relating to the SBC ODN's of *Kutyavin et al.* on page 6 of the Answer

were never expressed during prosecution. Nevertheless, under objection, Applicants address those arguments herein. Indeed, many of the passages of *Kutyavin et al.* cited by the Examiner support Applicants' contention that *Kutyavin et al.* do not teach or suggest all of the steps/features of the claims.

2. The Examiner has argued that the selective binding complementary ODNs (matched pair of ***oligonucleotides***) disclosed by *Kutyavin et al.* refer to those ODNs that contain nucleotide analog pairs. *See Office Action* at 5-6. As noted by the Examiner, *Kutyavin et al.* teach the following:

> In accordance with the present invention ***a matched pair of oligonucleotides*** (ODNs) are provided where each member of the pair is complementary or substantially complementary in the Watson Crick sense to a ***target duplex sequence***.... The ODNS of the invention... form substantially stable hybrids with the target sequence ***in each strand of duplex nucleic acid***.
>
> The ODNs of the present invention are termed Selective Binding Complementary (SBC) ODNs....
>
> [A] key feature of the SBC ODNs of the present invention is that ***each*** one of a matched pair of the SBC ODNs is complementary, or substantially complementary, to one target sequence in ***duplex*** nucleic acid wherein the target sequences are themselves complementary or substantially complementary to one another, and each one of the matched pair of SBC ODNs forms a stable hydrogen bonded hybrid with one strand of the target sequence.... ***Thus, the SBC ODNs are not hybridized to one another but they readily hybridize, especially ... when the target is in long double stranded DNA, with both strands of the target sequence.***

Kutyavin et al. at col. 1, lines 39-67 and col. 2, lines 14-31 (emphasis added). Applicants are fully aware of these teachings of *Kutyavin et al.* and indeed rely on them to make Applicants' arguments.

Attached as Exhibit "A" are two schemes that Applicants submit in response to the Examiner's arguments to help elucidate the present claims in view of the prior art and

demonstrate the novelty and nonobviousness of the claims in view of *Kutyavin et al.* Prior to *Kutyavin*, strand invasion of double-stranded DNA or RNA was typically accomplished via the incorporation of a ***single*** strand of an oligonucleotide into the double-stranded DNA or RNA. As demonstrated in Scheme A, *Kutyavin* discloses ***a matched set of oligonucleotides*** containing modified nucleotides, where each member of the set is able to hybridize with a complementary strand in a ***duplex nucleic acid molecule***, but is unable to hybridize with the other member of the matched set. Support for the characterization of the teachings of *Kutyavin et al.* as illustrated in Scheme B can be found in at least the following passages of *Kutyavin et al.* recited above.

In addition, *Kutyavin* refers to the modified SBC nucleotides at the following passage:

> ***A sufficient number of the modified SBC nucleotides are incorporated such that complementary positions in both SBC ODNS are modified into a matched pair of SBC ODNs of the present invention so that the pair of the matched set does not form a stable hybrid***.... It is not necessary to replace each natural nucleotide of the ODN with a modified SBC nucleotide in order to accomplish this. Both members of the matched pair are however complementary to a target sequence in double stranded or duplex nucleic acid, where the two strands or parts of the target duplex are themselves complementary or substantially complementary to one another. As it is described in more detail below, an important use of the SBC ODNs of the present invention is hybridization with secondary structure of mRNA wherein the mRNA itself forms a duplex, such as in hairpin loops.... The general concept of double stranded DNA and of secondary structure in mRNA and ribosomal RNA is covered in this description by the term "duplex nucleic acid".

Kutyavin at col. 4, lines 39-67 (emphasis added). In this passage, *Kutyavin et al.* is referring to the formation of ***probes*** in, for example, a hybridization assay. In contrast, as recited in claim 1, the nuclei acid molecules themselves are synthesized.

As illustrated in Scheme B, one embodiment of claim 1 includes providing a nucleic acid template and providing ***nucleotide precursors*** that have certain characteristics[1], such that when the nucleotides are polymerized to form an unstructured nucleic acid, the nucleotides have a reduced ability to form base pairs with each other. This is not the strand invasion of a ***duplex*** nucleic acid molecule as taught by *Kutyavin et al.* Two of the nucleic acid molecules synthesized by an embodiment of claim 1 are depicted in Scheme B to show how the nucleotide precursors of claim 1 have a reduced ability to form base pairs with each other. Support for the illustration in Scheme B can be found in the specification at least at pages 4-7, and for example, FIGs. 1G, 1H, and FIGs. 8A-8C and their attendant descriptions in the originally filed specification. Thus, not all the steps/features of claim 1 are taught or suggested by *Kutyavin et al.* For at least this reason, Applicants therefore respectfully request that the rejection of claim 1 be withdrawn.

Claim 12 also recites "providing nucleotide precursors that include pairs of complementary analog precursors that have a reduced ability to form base pairs with each other" and "contacting the first template and nucleotide precursors with an enzyme characterized by an ability to polymerize the precursors under conditions and for a time sufficient for synthesis of the first nucleic acid molecule," which is not taught or suggested by *Kutyavin et al.*

For at least this reason, Applicants therefore respectfully request that the rejection of claim 12 be withdrawn.

---

[1] Note that Scheme C uses the term "modified nucleotides." This term is merely for purposes of illustrating the concepts of Scheme C, as one embodiment, and not intended to limit the scope of claim. The term "nucleotide precursors" in claim 1 should be given its full scope and meaning in accordance with the specification as originally filed.

Claim 24 also recites "nucleotide precursors that include pairs of complementary analog precursors that have a reduced ability to form base pairs with each other" and "at least one enzyme capable of polymerizing the precursors into a polynucleotide molecule," which is not taught or suggested by *Kutyavin et al.* For at least this reason, Applicants therefore respectfully request that the rejection of claim 24 be withdrawn.

Applicants note that, insofar as claims 2-11, 13-23, and 25-26 depend, either directly or indirectly, from their respective independent claims 1, 12, and 24, claims 2-11, 13-23, and 25-26 are also not anticipated by *Kutyavin et al.*

No additional fees, except those that accompany this reply, are believed to be due in connection with this reply. If, however, any additional fees are deemed to be payable, you are hereby authorized to charge any such fees to deposit account number 50-1078.

Respectfully submitted,

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